

## SEQUENCE LISTING



<110> BLACK, Roy A.  
 PAXTON, Raymond J.  
 BODE, Wolfram  
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 FERNANDEZ-CATALAN, Carlos  
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 LEVIN, Jeremy Ian

<120> Crystalline TNF-alpha-converting enzyme  
 and uses thereof

<130> 16163-039004

<140> US 10/784,300

<141> 2004-02-24

<150> US 09/244,984

<151> 1999-02-04

<150> US 60/073,709

<151> 1998-02-04

<150> US 60/135,499

<151> 1998-03-30

<150> US 60/117,476

<151> 1999-01-27

<160> 11

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Illustrative peptide

<400> 1

Pro	Leu	Ala	Gln	Ala	Val	Arg	Ser	Ser	Ser
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<210> 2

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Illustrative peptide

&lt;400&gt; 2

Gly Ser His His His His His His

1

5

&lt;210&gt; 3

&lt;211&gt; 11

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Consensus motif

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; 3, 4, 6, 7, 9, 10

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 3

His Glu Xaa Xaa His Xaa Xaa Gly Xaa Xaa His

1

5

10

&lt;210&gt; 4

&lt;211&gt; 203

&lt;212&gt; PRT

&lt;213&gt; Crotalus adamanteus

&lt;400&gt; 4

Glu Gln Asn Leu Pro Gln Arg Tyr Ile Glu Leu Val Val Val Ala Asp

1

5

10

15

Arg Arg Val Phe Met Lys Tyr Asn Ser Asp Leu Asn Ile Ile Arg Thr

20

25

30

Arg Val His Glu Ile Val Asn Ile Ile Asn Glu Phe Tyr Arg Ser Leu

35

40

45

Asn Ile Arg Val Ser Leu Thr Asp Leu Glu Ile Trp Ser Gly Gln Asp

50

55

60

Phe Ile Thr Ile Gln Ser Ser Ser Ser Asn Thr Leu Asn Ser Phe Gly

65

70

75

80

Glu Trp Arg Glu Arg Val Leu Leu Thr Arg Lys Arg His Asp Asn Ala

85

90

95

Gln Leu Leu Thr Ala Ile Asn Phe Glu Gly Lys Ile Ile Gly Lys Ala

100

105

110

Tyr Thr Ser Ser Met Cys Asn Pro Arg Ser Ser Val Gly Ile Val Lys

115

120

125

Asp His Ser Pro Ile Asn Leu Val Ala Val Thr Met Ala His Glu

130

135

140

Leu Gly His Asn Leu Gly Met Glu His Asp Gly Lys Asp Cys Leu Arg

145

150

155

160

Gly Ala Ser Leu Cys Ile Met Arg Pro Gly Leu Thr Pro Gly Arg Ser

165

170

175

Tyr Glu Phe Ser Asp Asp Ser Met Gly Tyr Tyr Gln Lys Phe Leu Asn

180

185

190

Gln Tyr Lys Pro Gln Cys Ile Leu Asn Lys Pro

195

200

<210> 5  
 <211> 287  
 <212> PRT  
 <213> Homo sapiens

<400> 5  
 Pro Glu Glu Leu Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro  
 1 5 10 15  
 Met Lys Asn Thr Cys Lys Leu Leu Val Ala Asp His Arg Phe Tyr  
 20 25 30  
 Arg Tyr Met Gly Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile  
 35 40 45  
 Glu Leu Ile Asp Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp  
 50 55 60  
 Asn Ala Gly Phe Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile  
 65 70 75 80  
 Leu Lys Ser Pro Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met  
 85 90 95  
 Ala Lys Ser Tyr Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met  
 100 105 110  
 Leu Leu Glu Gln Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val  
 115 120 125  
 Cys Leu Ala His Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu  
 130 135 140  
 Gly Leu Ala Tyr Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val  
 145 150 155 160  
 Cys Pro Lys Ser Gly Ser Ser Gly Gly Ile Cys Glu Lys Ala Tyr Tyr  
 165 170 175  
 Ser Pro Val Gly Lys Lys Asn Ser Lys Leu Tyr Ser Asp Gly Lys Lys  
 180 185 190  
 Lys Glu Ala Asp Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly  
 195 200 205  
 Ala Glu His Asp Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp  
 210 215 220  
 Gln Gly Gly Lys Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His  
 225 230 235 240  
 Glu Asn Asn Lys Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys  
 245 250 255  
 Thr Ile Glu Ser Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys  
 260 265 270  
 Val Cys Gly Asn Ser Arg Val Asp Glu Gly Glu Glu Cys Asp Pro  
 275 280 285

<210> 6  
 <211> 276  
 <212> PRT  
 <213> Homo sapiens

<400> 6  
 Gln Glu Lys His Ala Ile Asn Gly Pro Glu Leu Leu Arg Lys Arg Arg  
 1 5 10 15  
 Thr Thr Ser Ala Glu Lys Asn Thr Cys Gln Leu Tyr Ile Gln Thr Asp  
 20 25 30  
 His Leu Phe Phe Lys Tyr Tyr Gly Thr Arg Glu Ala Val Ile Ala Gln  
 35 40 45  
 Ile Ser Ser His Val Lys Ala Ile Asp Thr Ile Tyr Gln Thr Thr Asp

50		55		60											
Phe	Ser	Gly	Ile	Arg	Asn	Ile	Ser	Phe	Met	Val	Lys	Arg	Ile	Arg	Ile
65					70					75					80
Asn	Thr	Thr	Ala	Asp	Glu	Lys	Asp	Pro	Thr	Asn	Pro	Phe	Arg	Phe	Pro
				85					90					95	
Asn	Ile	Ser	Val	Glu	Lys	Phe	Leu	Glu	Leu	Asn	Ser	Glu	Gln	Asn	His
			100					105					110		
Asp	Asp	Tyr	Cys	Leu	Ala	Tyr	Val	Phe	Thr	Asp	Arg	Asp	Phe	Asp	Asp
		115					120					125			
Gly	Val	Leu	Gly	Leu	Ala	Trp	Val	Gly	Ala	Pro	Ile	Tyr	Leu	Asn	Ser
	130					135					140				
Gly	Leu	Thr	Ser	Thr	Ser	Leu	Asn	Thr	Gly	Ile	Ile	Thr	Val	Lys	Asn
145					150					155					160
Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Gln	Asn	Tyr	Gly	Ser	His	Val	Pro
			165						170					175	
Pro	Lys	Val	Ser	His	Ile	Thr	Phe	Ala	His	Glu	Val	Gly	His	Asn	Phe
			180				185					190			
Gly	Ser	Pro	His	Asp	Ser	Gly	Thr	Glu	Cys	Thr	Pro	Gly	Glu	Ser	Lys
	195					200						205			
Asn	Leu	Gly	Gln	Lys	Glu	Asn	Gly	Asn	Tyr	Ile	Met	Tyr	Ala	Arg	Ala
	210					215					220				
Thr	Ser	Gly	Asp	Lys	Leu	Asn	Asn	Asn	Lys	Phe	Ser	Leu	Cys	Ser	Ile
225					230					235					240
Arg	Asn	Ile	Ser	Gln	Val	Leu	Glu	Lys	Lys	Arg	Asn	Asn	Cys	Phe	Val
			245					250					255		
Glu	Ser	Gly	Gln	Pro	Ile	Cys	Gly	Asn	Gly	Met	Val	Glu	Gln	Gly	Glu
		260					265					270			
Glu	Cys	Asp	Cys												
	275														

&lt;210&gt; 7

&lt;211&gt; 824

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 7

Met	Arg	Gln	Ser	Leu	Leu	Phe	Leu	Thr	Ser	Val	Val	Pro	Phe	Val	Leu
1				5					10					15	
Ala	Pro	Arg	Pro	Pro	Asp	Asp	Pro	Gly	Phe	Gly	Pro	His	Gln	Arg	Leu
			20					25					30		
Glu	Lys	Leu	Asp	Ser	Leu	Leu	Ser	Asp	Tyr	Asp	Ile	Leu	Ser	Leu	Ser
		35					40					45			
Asn	Ile	Gln	Gln	His	Ser	Val	Arg	Lys	Arg	Asp	Leu	Gln	Thr	Ser	Thr
	50					55					60				
His	Val	Glu	Thr	Leu	Leu	Thr	Phe	Ser	Ala	Leu	Lys	Arg	His	Phe	Lys
65					70					75					80
Leu	Tyr	Leu	Thr	Ser	Ser	Thr	Glu	Arg	Phe	Ser	Gln	Asn	Phe	Lys	Val
			85						90					95	
Val	Val	Val	Asp	Gly	Lys	Asn	Glu	Ser	Glu	Tyr	Thr	Ala	Lys	Trp	Gln
		100					105						110		
Asp	Phe	Phe	Thr	Gly	His	Val	Val	Gly	Glu	Pro	Asp	Ser	Arg	Val	Leu
		115					120				125				
Ala	His	Ile	Arg	Asp	Asp	Asp	Val	Ile	Ile	Arg	Ile	Asn	Thr	Asp	Gly
	130					135					140				
Ala	Glu	Tyr	Asn	Ile	Glu	Pro	Leu	Trp	Arg	Phe	Val	Asn	Asp	Thr	Lys
145					150					155					160

Asp	Lys	Arg	Met	Leu	Val	Tyr	Lys	Ser	Glu	Asp	Ile	Lys	Asn	Val	Ser	165	170	175
Arg	Leu	Gln	Ser	Pro	Lys	Val	Cys	Gly	Tyr	Leu	Lys	Val	Asp	Asn	Glu	180	185	190
Glu	Leu	Leu	Pro	Lys	Gly	Leu	Val	Asp	Arg	Glu	Pro	Pro	Glu	Glu	Leu	195	200	205
Val	His	Arg	Val	Lys	Arg	Arg	Ala	Asp	Pro	Asp	Pro	Met	Lys	Asn	Thr	210	215	220
Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg	Phe	Tyr	Arg	Tyr	Met	Gly	225	230	235
Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr	Leu	Ile	Glu	Leu	Ile	Asp	245	250	255
Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ser	Trp	Asp	Asn	Ala	Gly	Phe	260	265	270
Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile	Arg	Ile	Leu	Lys	Ser	Pro	275	280	285
Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr	Asn	Met	Ala	Lys	Ser	Tyr	290	295	300
Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val	Lys	Met	Leu	Leu	Glu	Gln	305	310	315
Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser	Lys	Val	Cys	Leu	Ala	His	325	330	335
Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly	Thr	Leu	Gly	Leu	Ala	Tyr	340	345	350
Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly	Gly	Val	Cys	Pro	Lys	Ala	355	360	365
Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile	Tyr	Leu	Asn	Ser	Gly	Leu	370	375	380
Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile	Leu	Thr	Lys	Glu	Ala	Asp	385	390	395
Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn	Phe	Gly	Ala	Glu	His	Asp	405	410	415
Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn	Glu	Asp	Gln	Gly	Gly	Lys	420	425	430
Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly	Asp	His	Glu	Asn	Asn	Lys	435	440	445
Met	Phe	Ser	Asn	Cys	Ser	Lys	Gln	Ser	Ile	Tyr	Lys	Thr	Ile	Glu	Ser	450	455	460
Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser	Asn	Lys	Val	Cys	Gly	Asn	465	470	475
Ser	Arg	Val	Asp	Glu	Gly	Glu	Glu	Cys	Asp	Pro	Gly	Ile	Met	Tyr	Leu	485	490	495
Asn	Asn	Asp	Thr	Cys	Cys	Asn	Ser	Asp	Cys	Thr	Leu	Lys	Glu	Gly	Val	500	505	510
Gln	Cys	Ser	Asp	Arg	Asn	Ser	Pro	Cys	Cys	Lys	Asn	Cys	Gln	Phe	Glu	515	520	525
Thr	Ala	Gln	Lys	Lys	Cys	Gln	Glu	Ala	Ile	Asn	Ala	Thr	Cys	Lys	Gly	530	535	540
Val	Ser	Tyr	Cys	Thr	Gly	Asn	Ser	Ser	Glu	Cys	Pro	Pro	Pro	Gly	Asn	545	550	555
Ala	Glu	Asn	Asp	Thr	Val	Cys	Leu	Asp	Leu	Gly	Lys	Cys	Lys	Asp	Gly	565	570	575
Lys	Cys	Ile	Pro	Phe	Cys	Glu	Arg	Glu	Gln	Gln	Leu	Glu	Ser	Cys	Ala	580	585	590
Cys	Asn	Glu	Thr	Asp	Asn	Ser	Cys	Lys	Val	Cys	Cys	Arg	Asp	Leu	Ser	595	600	605
Gly	Arg	Cys	Val	Pro	Tyr	Val	Asp	Ala	Glu	Gln	Lys	Asn	Leu	Phe	Leu			

610	615	620
Arg Lys Gly Lys Pro Cys Thr Val Gly Phe Cys Asp Met Asn Gly Lys		
625	630	635
Cys Glu Lys Arg Val Gln Asp Val Ile Glu Arg Phe Trp Asp Phe Ile		640
	645	650
Asp Gln Leu Ser Ile Asn Thr Phe Gly Lys Phe Leu Ala Asp Asn Ile		655
	660	665
Val Gly Ser Val Leu Val Phe Ser Leu Ile Phe Trp Ile Pro Phe Ser		670
	675	680
Ile Leu Val His Cys Val Asp Lys Lys Leu Asp Lys Gln Tyr Glu Ser		685
	690	695
Leu Ser Leu Phe His Pro Ser Asn Val Glu Met Leu Ser Ser Met Asp		700
705	710	715
Ser Ala Ser Val Arg Ile Ile Lys Pro Phe Pro Ala Pro Gln Thr Pro		720
	725	730
Gly Arg Leu Gln Pro Ala Pro Val Ile Pro Ser Ala Pro Ala Ala Pro		735
	740	745
Lys Leu Asp His Gln Arg Met Asp Thr Ile Gln Glu Asp Pro Ser Thr		750
	755	760
Asp Ser His Met Asp Glu Asp Gly Phe Glu Lys Asp Pro Phe Pro Asn		765
	770	775
Ser Ser Thr Ala Ala Lys Ser Phe Glu Asp Leu Thr Asp His Pro Val		780
785	790	795
Ala Arg Ser Glu Lys Ala Ala Ser Phe Lys Leu Gln Arg Gln Asn Arg		800
	805	810
Val Asn Ser Lys Glu Thr Glu Cys		815
	820	

&lt;210&gt; 8

&lt;211&gt; 477

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 8

Met Arg Gln Ser Leu Leu Phe Leu Thr Ser Val Val Pro Phe Val Leu	
1	5
Ala Pro Arg Pro Pro Asp Asp Pro Gly Phe Gly Pro His Gln Arg Leu	10
	15
	20
Glu Lys Leu Asp Ser Leu Leu Ser Asp Tyr Asp Ile Leu Ser Leu Ser	25
	30
	35
Asn Ile Gln Gln His Ser Val Arg Lys Arg Asp Leu Gln Thr Ser Thr	40
	45
	50
His Val Glu Thr Leu Leu Thr Phe Ser Ala Leu Lys Arg His Phe Lys	55
65	60
	65
Leu Tyr Leu Thr Ser Ser Thr Glu Arg Phe Ser Gln Asn Phe Lys Val	70
	75
	80
	85
Val Val Val Asp Gly Lys Asn Glu Ser Glu Tyr Thr Val Lys Trp Gln	90
	95
	100
Asp Phe Phe Thr Gly His Val Val Gly Glu Pro Asp Ser Arg Val Leu	105
	110
	115
Ala His Ile Arg Asp Asp Asp Val Ile Ile Arg Ile Asn Thr Asp Gly	120
	125
	130
Ala Glu Tyr Asn Ile Glu Pro Leu Trp Arg Phe Val Asn Asp Thr Lys	135
145	140
	145
Asp Lys Arg Met Leu Val Tyr Lys Ser Glu Asp Ile Lys Asn Val Ser	150
	155
	160
	165
	170
	175

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Arg Leu Gln Ser Pro Lys Val Cys Gly Tyr Leu Lys Val Asp Asn Glu
      180      185      190
Glu Leu Leu Pro Lys Gly Leu Val Asp Arg Glu Pro Pro Glu Glu Leu
      195      200      205
Val His Arg Val Lys Arg Arg Ala Asp Pro Asp Pro Met Lys Asn Thr
      210      215      220
Cys Lys Leu Leu Val Val Ala Asp His Arg Phe Tyr Arg Tyr Met Gly
225      230      235      240
Arg Gly Glu Glu Ser Thr Thr Thr Asn Tyr Leu Ile Glu Leu Ile Asp
      245      250      255
Arg Val Asp Asp Ile Tyr Arg Asn Thr Ser Trp Asp Asn Ala Gly Phe
      260      265      270
Lys Gly Tyr Gly Ile Gln Ile Glu Gln Ile Arg Ile Leu Lys Ser Pro
      275      280      285
Gln Glu Val Lys Pro Gly Glu Lys His Tyr Asn Met Ala Lys Ser Tyr
      290      295      300
Pro Asn Glu Glu Lys Asp Ala Trp Asp Val Lys Met Leu Leu Glu Gln
305      310      315      320
Phe Ser Phe Asp Ile Ala Glu Glu Ala Ser Lys Val Cys Leu Ala His
      325      330      335
Leu Phe Thr Tyr Gln Asp Phe Asp Met Gly Thr Leu Gly Leu Ala Tyr
      340      345      350
Val Gly Ser Pro Arg Ala Asn Ser His Gly Gly Val Cys Pro Lys Ala
      355      360      365
Tyr Tyr Ser Pro Val Gly Lys Lys Asn Ile Tyr Leu Asn Ser Gly Leu
      370      375      380
Thr Ser Thr Lys Asn Tyr Gly Lys Thr Ile Leu Thr Lys Glu Ala Asp
385      390      395      400
Leu Val Thr Thr His Glu Leu Gly His Asn Phe Gly Ala Glu His Asp
      405      410      415
Pro Asp Gly Leu Ala Glu Cys Ala Pro Asn Glu Asp Gln Gly Gly Lys
      420      425      430
Tyr Val Met Tyr Pro Ile Ala Val Ser Gly Asp His Glu Asn Asn Lys
      435      440      445
Met Phe Ser Asn Cys Ser Lys Gln Ser Ile Tyr Lys Thr Ile Glu Ser
      450      455      460
Lys Ala Gln Glu Cys Phe Gln Glu Arg Ser Asn Lys Val
465      470      475

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<210> 9

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetically generated peptide

<400> 9

Ser Pro Leu Ala Gln Ala Val Arg Ser Ser Ser Arg

1

5

10

<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Illustrative Met-turn located in SEQ ID NOS 5 and  
6

<400> 10

Tyr Val Met Tyr

1

<210> 11

<211> 256

<212> PRT

<213> Homo sapiens

<400> 11

Asp	Pro	Met	Lys	Asn	Thr	Cys	Lys	Leu	Leu	Val	Val	Ala	Asp	His	Arg
1				5					10					15	
Phe	Tyr	Arg	Tyr	Met	Gly	Arg	Gly	Glu	Glu	Ser	Thr	Thr	Thr	Asn	Tyr
			20					25					30		
Leu	Ile	Glu	Leu	Ile	Asp	Arg	Val	Asp	Asp	Ile	Tyr	Arg	Asn	Thr	Ala
		35					40					45			
Trp	Asp	Asn	Ala	Gly	Phe	Lys	Gly	Tyr	Gly	Ile	Gln	Ile	Glu	Gln	Ile
	50					55				60					
Arg	Ile	Leu	Lys	Ser	Pro	Gln	Glu	Val	Lys	Pro	Gly	Glu	Lys	His	Tyr
65					70				75					80	
Asn	Met	Ala	Lys	Ser	Tyr	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Trp	Asp	Val
			85						90					95	
Lys	Met	Leu	Leu	Glu	Gln	Phe	Ser	Phe	Asp	Ile	Ala	Glu	Glu	Ala	Ser
		100						105				110			
Lys	Val	Cys	Leu	Ala	His	Leu	Phe	Thr	Tyr	Gln	Asp	Phe	Asp	Met	Gly
		115					120				125				
Thr	Leu	Gly	Leu	Ala	Tyr	Val	Gly	Ser	Pro	Arg	Ala	Asn	Ser	His	Gly
	130					135				140					
Gly	Val	Cys	Pro	Lys	Ala	Tyr	Tyr	Ser	Pro	Val	Gly	Lys	Lys	Asn	Ile
145					150					155				160	
Tyr	Leu	Asn	Ser	Gly	Leu	Thr	Ser	Thr	Lys	Asn	Tyr	Gly	Lys	Thr	Ile
			165						170					175	
Leu	Thr	Lys	Glu	Ala	Asp	Leu	Val	Thr	Thr	His	Glu	Leu	Gly	His	Asn
		180						185				190			
Phe	Gly	Ala	Glu	His	Asp	Pro	Asp	Gly	Leu	Ala	Glu	Cys	Ala	Pro	Asn
	195					200					205				
Glu	Asp	Gln	Gly	Gly	Lys	Tyr	Val	Met	Tyr	Pro	Ile	Ala	Val	Ser	Gly
	210					215				220					
Asp	His	Glu	Asn	Asn	Lys	Met	Phe	Ser	Gln	Cys	Ser	Lys	Gln	Ser	Ile
225					230					235				240	
Tyr	Lys	Thr	Ile	Glu	Ser	Lys	Ala	Gln	Glu	Cys	Phe	Gln	Glu	Arg	Ser
			245					250						255	